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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,097	06/14/2001	Anton Wellstein	GUH-025-101	3830

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EXAMINER	
KOLKER, DANIEL E	

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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/880,097	WELLSTEIN, ANTON	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95,96,99-101 and 103-127* is/are pending in the application.

4a) Of the above claim(s) *106-118* is/are withdrawn from consideration.

5)☒ Claim(s) *95,96,99-101,104,119,120 and 122* is/are allowed.

6)☒ Claim(s) *103,105,121 and 123-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 2 June 2008 have been entered. Claims 95 – 96, 99 – 101, and 103 – 127 are pending.

Election/Restrictions

2. Claims 106 – 118 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2 February 2004.

3. This application contains claims 106 – 118 drawn to an invention nonelected with traverse in the reply filed on 2 February 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. Claims 95 – 96, 99 – 101, 103 – 105, and 119 – 127 are under examination.

Withdrawn Rejections

5. The rejection of claims 103 and 121 under 35 USC 112, second paragraph is withdrawn in light of the amendments which clarify that the compositions comprise polypeptides present in an amount effective for the stimulation of desired cell proliferation.

Maintained Rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 105 and 123 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection stands for the reasons previously made of record and explained in further detail below. As set forth in the office action mailed 31 January 2008 at pp. 4 – 5, the specification fails to disclose the structure of the test substances included in the compositions of claims 105 and 123. While the substances have the function of blocking the binding of PTN with ALK, the specification fails to disclose actual structure of a representative number of members of this genus of structurally unrelated products. Applicant argues, at p. 7 of the remarks filed 2 June 2008, that the rejection should be withdrawn as the specification shows actual reduction to practice of a few members of the genus, including anti-PTN and anti-ALK extracellular domain (ECD) antibodies, as well as recombinant ALK ECD and unlabeled PTN.

Applicant's arguments have been fully considered but they are not persuasive. The claims are not limited to compositions comprising the polypeptide of claim 95 with PTN, ALK, and an agent selected from the group consisting of anti-PTN antibodies, anti-ALK ECD antibodies recombinant ALK ECD and unlabeled PTN. The claims encompass compositions which include any and all test substances, defined in the specification to "include most any substance such as, for example, antibodies… drugs, anti-angiogenic substances... anti-proliferative and proliferative substances,… biologically active substances and combinations thereof." (specification, p. 14 lines 19 – 26) The specification fails to disclose to the public the structures common to all members of this wide genus which allow them to block binding of PTN with ALK. The specification describes no anti-neoplastic, anti-tumorigenic, or anti-motogenic substances which have this property. The specification discloses no drugs which have this property. The disclosure of two antibodies and two proteins (ALK and PTN) that block binding is not representative of the genus of test substances recited in the claims.

Applicant is directed to the newly-issued guidelines for interpretation of the written description requirement of 35 USC 112, first paragraph, available on the office's website at http://www.uspto.gov/web/menu/written.pdf . See in particular p. 1, which discusses the requirement in general, and Example 17 beginning on p. 58, which is similar to this situation. As the specification does not provide evidence of possession of the compositions comprising the full genus of test compounds which block binding of PTN to ALK, claims 105 and 123 stand rejected.

Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

7. Claims 103, 121, and 124 – 127 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the polypeptide of claim 95, does not reasonably provide enablement for therapeutically effective amounts of same effective for stimulation of cell proliferation as claimed, or for complete prevention of undesired proliferation as encompassed by claims 124 – 125, or for induction of apoptosis as recited in claims 126 – 127. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

The nature of the invention is complex. The claims are drawn to polypeptides and compositions comprising same wherein the polypeptide is present in an amount effective to either stimulate (claims 103 and 121) or alternatively prevent (claims 124 – 125) cell proliferation. The claims therefore encompass compositions with mutually exclusive possible concentrations of the polypeptide. Those concentrations which are effective to stimulate proliferation will not be able to prevent proliferation, and those concentrations which are effective to prevent proliferation will not, by definition, be able to stimulate it.

The claims are drawn to compositions comprising part but not all of ALK protein. Note independent claim 95 specifically recites which regions of ALK are present, and states that “said recombinant protein does not comprise further regions of ALK". Additionally, the claimed polypeptide must include the pleiotrophin (PTN)-binding region. Clearly the claimed products read on compositions comprising PTN-binding fragments of ALK, but not on full-length ALK proteins. The specification identifies ALK as a receptor that binds to PTN and transduces a signal (see Example 7). However since the claimed products do not include the signal-transducing region of ALK, they will bind to PTN but will not allow the appropriate signal to be

transduced. That is, the ALK fragments will act like anti-PTN antibodies, in that they will bind to PTN and inhibit its activity. Since the ALK fragments will not be able to transduce a signal, they will not be able to induce apoptosis as recited in claims 126 – 127, or in fact any intracellular effect. Additionally, the specification provides no evidence or working examples of compositions comprising PTN-binding regions of ALK but not other regions of ALK which actually do induce apoptosis as claimed. Thus the skilled artisan would have to determine which concentrations of the polypeptide of claim 95 in fact are sufficient to induce apoptosis. Given the lack of guidance in the specification, this degree of experimentation would be undue.

At the time the invention was made, the art recognized that PTN induced cell proliferation. See for example Sato 1999 (Experimental Cell Research 246:152-164), who teaches that "pleiotrophin is a new potent growth factor" and that the data indicate "a biological significance of pleiotrophin in the proliferation of hepatocytes in vitro" (see abstract; see also p. 163 first column). Additionally Dreyfus 1998 (Experimental Cell Research 241:171-180) teaches that pleiotrophin stimulate cell proliferation in a different experimental system. Thus the skilled artisan would recognize that the effect of the claimed compositions would be to attenuate the proliferation-inducing effects of PTN, since the ALK fragments would act like anti-PTN antibodies

The specification offers no working examples of compositions that stimulate proliferation, as encompassed by claims 103 and 121. The specification fails to provide guidance as to how to transform the compositions, which would be expected to be inhibitory rather than stimulatory, into proliferation-stimulating compositions as claimed. Thus the skilled artisan would have to resort to painstaking experimentation in order to determine how to reverse the function of the claimed compositions. Given the lack of guidance in the specification, such experimentation would be undue.

Additionally, the specification is not enabling for complete prevention of undesired proliferation as claimed. While it is reasonable that the compositions would have the effect of attenuating proliferation, the full scope of claims 124 – 125 includes total prevention of all undesired proliferation. That is, the claims encompass methods where a single instance of undesired cell division never occurs. This is generally recognized as impossible, and the specification fails to provide evidence that such a goal is actually achieved. The skilled artisan would have to resort to a very large degree of experimentation in order to determine which concentrations of the claimed polypeptides are sufficient to prevent all undesired proliferation.

Coupled with the lack of guidance in the specification and the fact that the skilled artisan would recognize that total prevention is generally not possible, the large degree of experimentation required would be undue.

Conclusion

8. Claims 95 – 96, 99 – 101, 104, 119 – 120, and 122 are allowed.

9. Claims 103, 105, 121, and 123 – 127 are rejected.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker, Ph.D./
Patent Examiner, Art Unit 1649
September 4, 2008